

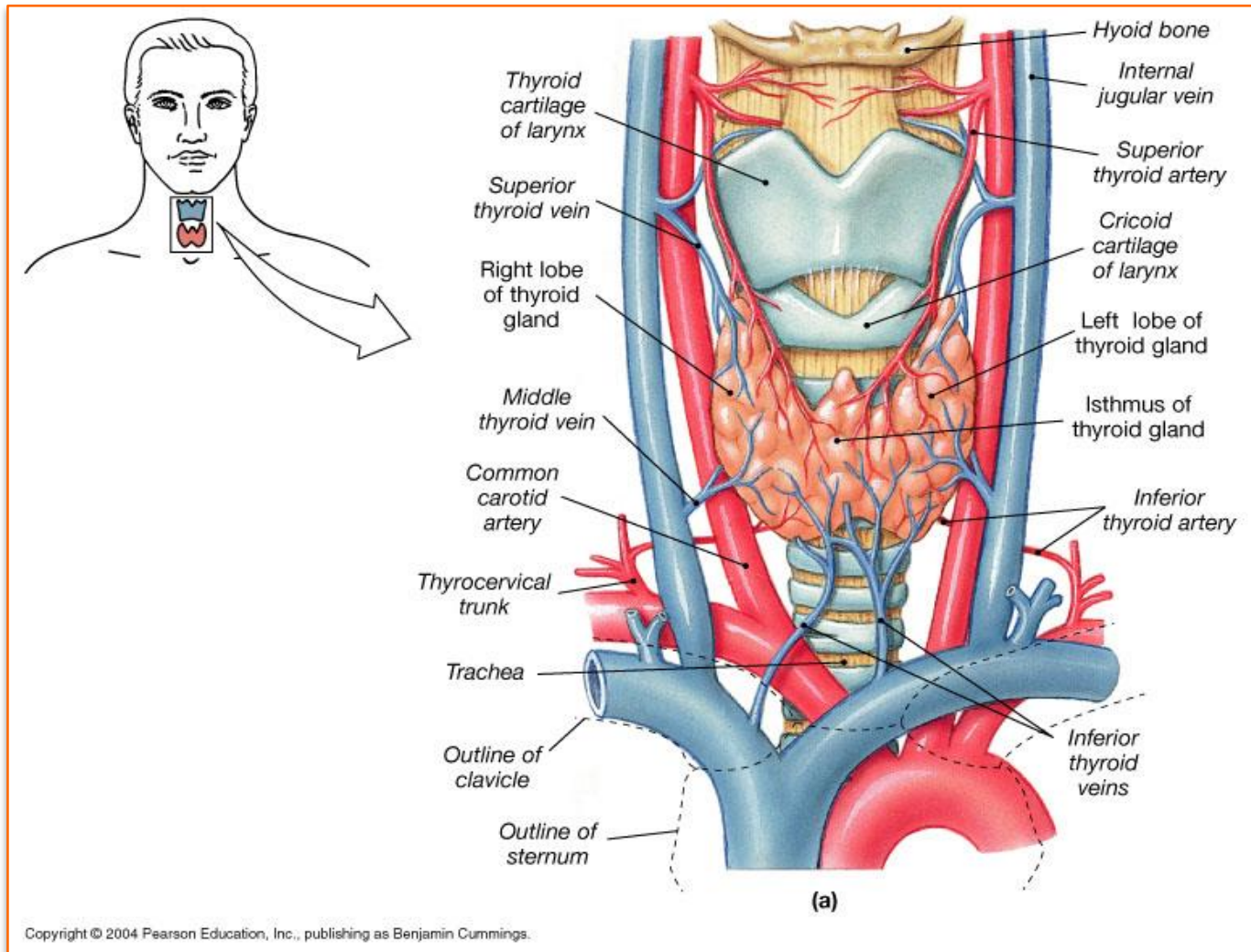
DISORDERS OF THE THYROID GLAND

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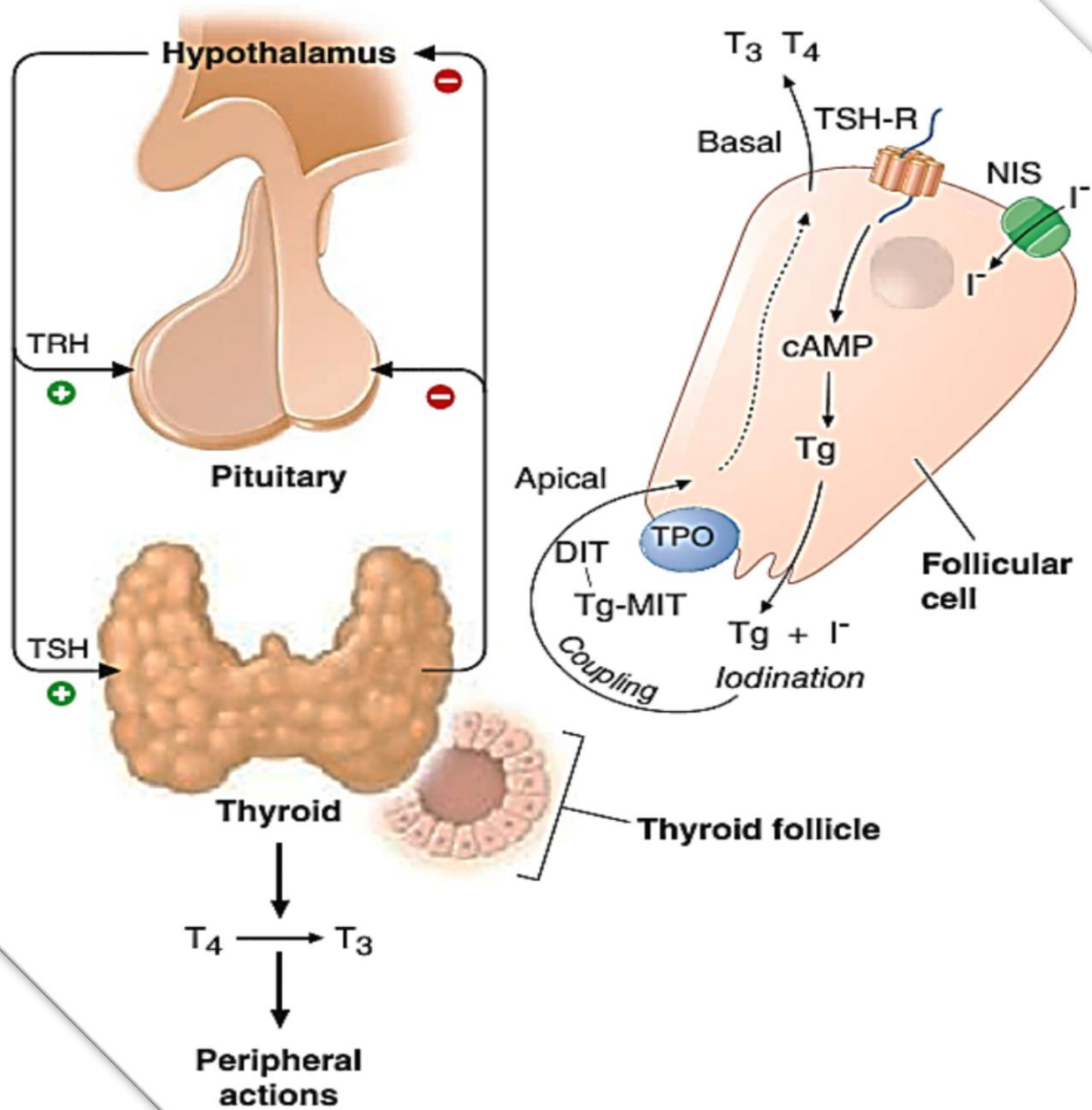
- The normal thyroid is 12–20 g in size, highly vascular, and soft in consistency and consists of two lobes connected by an isthmus...

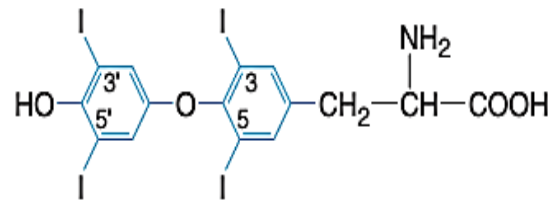


Regulation of thyroid hormone synthesis

- **TSH** is the dominant hormonal regulator of thyroid gland growth and function...its highest levels occur at night....
- A variety of **growth factors**, most produced locally in the thyroid gland, also influence thyroid hormone synthesis...
- Cytokines and interleukins...
- IGF-1...
- Iodine excess & deficiency...







Thyroxine (T₄)
3,5,3',5'-Tetraiodothyronine

Hormone Property	T ₄	T ₃
Serum concentrations		
Total hormone	8 µg/dL	0.14 µg/dL
Fraction of total hormone in the unbound form	0.02%	0.3%
Unbound (free) hormone	$21 \times 10^{-12}M$	$6 \times 10^{-12}M$
Serum half-life	7 d	2 d
Fraction directly from the thyroid	100%	20%
Production rate, including peripheral conversion	90 µg/d	32 µg/d
Intracellular hormone fraction	~20%	~70%
Relative metabolic potency	0.3	1
Receptor binding	$10^{-10}M$	$10^{-11}M$

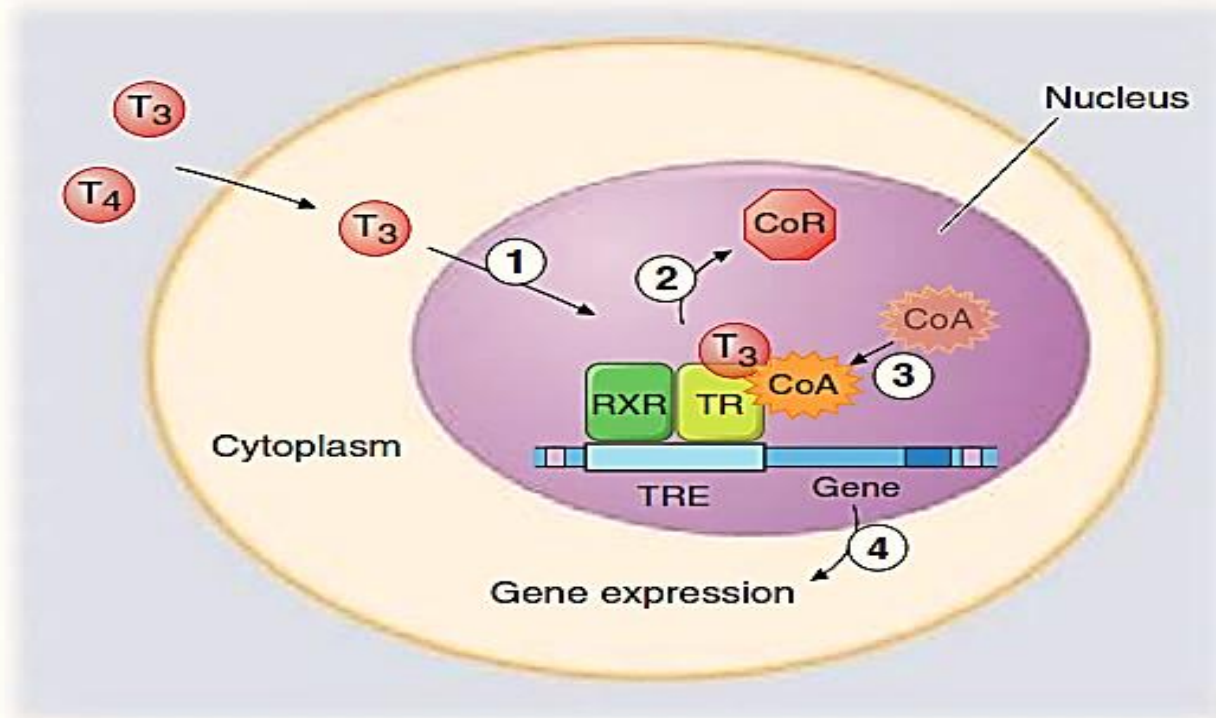


FIGURE 405-4 Mechanism of thyroid hormone receptor action.

The thyroid hormone receptor (TR) and retinoid X receptor (RXR) form heterodimers that bind specifically to thyroid hormone response elements (TRE) in the promoter regions of target genes. In the absence of hormone, TR binds co-repressor (CoR) proteins that silence gene expression. The numbers refer to a series of ordered reactions that occur in response to thyroid hormone: (1) T_4 or T_3 enters the nucleus; (2) T_3 binding dissociates CoR from TR; (3) co-activators (CoA) are recruited to the T_3 -bound receptor; and (4) gene expression is altered.

THYROID EVALUATION

- ❖ Determining serum **thyroid hormone levels**...
- ❖ Measuring thyroid **autoantibodies**...
- ❖ **Imaging** thyroid gland size and architecture...
- ❖ Performing a **thyroid gland biopsy** (FNA)...



THYROID HORMONE LEVELS

- Serum TSH is measured by a third-generation immuno-metric assay and Total serum T4 and T3 by radioimmunoassay...
- The plasma-binding proteins; increase the pool of circulating hormone, delay hormone clearance, and may modulate hormone delivery to selected tissue sites...including:
 - ✓ Thyroxine-binding globulin (TBG)
 - ✓ Transthyretin (TTR)
 - ✓ Albumin...



❑ Two **direct** methods are used to measure unbound thyroid hormones :

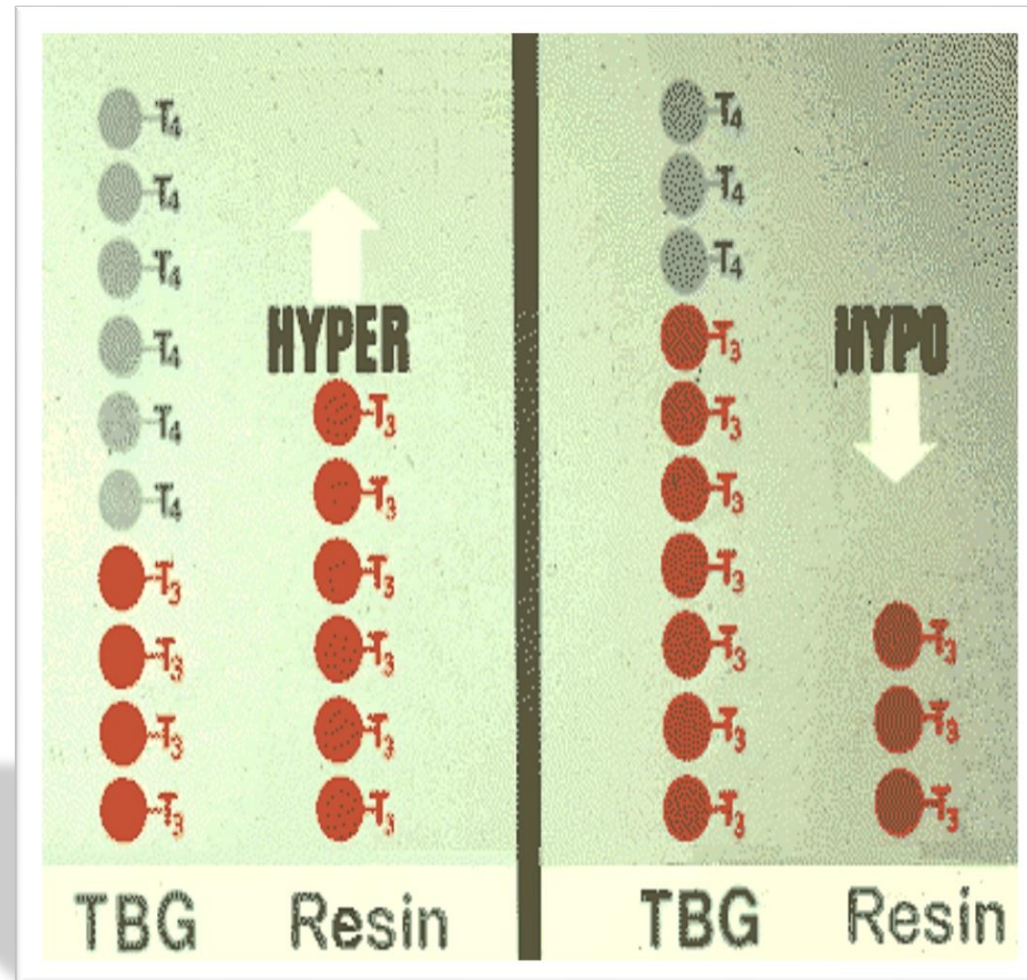
1) unbound thyroid hormone **competition** with radiolabeled T4 (or an analogue) for binding to a solid-phase antibody...

2) physical **separation** of the unbound hormone fraction by ultracentrifugation or equilibrium dialysis...

❑ An **indirect** method that is now less commonly used to estimate unbound thyroid hormone levels is to calculate the free T3 or free T4 index from the total T4 or T3 concentration and the thyroid hormone binding ratio (**THBR**).



- The latter is derived from the **T3-resin uptake test**, which determines the distribution of radiolabeled T3 between an absorbent resin and the unoccupied thyroid hormone binding proteins in the sample...



Abnormalities of Thyroid Hormone Binding Proteins

Disorder	Cause	Transmission	Characteristics
Familial dysalbuminemic hyperthyroxinemia (FDH)	Albumin mutations, usually R218H	AD	Increased T_4 Normal unbound T_4 Rarely increased T_3
TBG			
Familial excess	Increased TBG production	XL	Increased total T_4, T_3 Normal unbound T_4, T_3
Acquired excess	Medications (estrogen), pregnancy, cirrhosis, hepatitis	Acquired	Increased total T_4, T_3 Normal unbound T_4, T_3
Transthyretin ^a			
Excess	Islet tumors	Acquired	Usually normal T_4, T_3
Mutations	Increased affinity for T_4 or T_3	AD	Increased total T_4, T_3 Normal unbound T_4, T_3
Medications: propranolol, ipodate, iopanoic acid, amiodarone	Decreased $T_4 \rightarrow T_3$ conversion	Acquired	Increased T_4 Decreased T_3 Normal or increased TSH
Resistance to thyroid hormone (RTH)	Thyroid hormone receptor β mutations	AD	Increased unbound T_4, T_3 Normal or increased TSH Some patients clinically thyrotoxic

^aAlso known as thyroxine-binding prealbumin (TBPA).

Thyroid Autoantibodies

- About 5–15% of euthyroid women and up to 2% of euthyroid men have thyroid antibodies; such individuals are at **increased risk** of developing thyroid dysfunction...
- Almost all patients with autoimmune hypothyroidism, and up to **80%** of those with **Graves'** disease, have **TPO antibodies**, usually at high levels.
- **TSIs** are antibodies that stimulate the TSH-R in Graves' disease...(TRAb)
- The **main use** of these assays is to predict neonatal thyrotoxicosis caused by high maternal levels of TRAb or TSI (**> 3 × upper** limit of normal) in the last trimester of pregnancy....



- Serum Tg levels are increased in all types of thyrotoxicosis **except** thyrotoxicosis **factitia** caused by self-administration of thyroid hormone....
- Tg levels are particularly increased in thyroiditis, reflecting thyroid tissue destruction and release of Tg...
- The **main role for Tg** measurement, however, is in the follow-up of thyroid **cancer** patients...



TFT IN HYPOTHYROIDISM

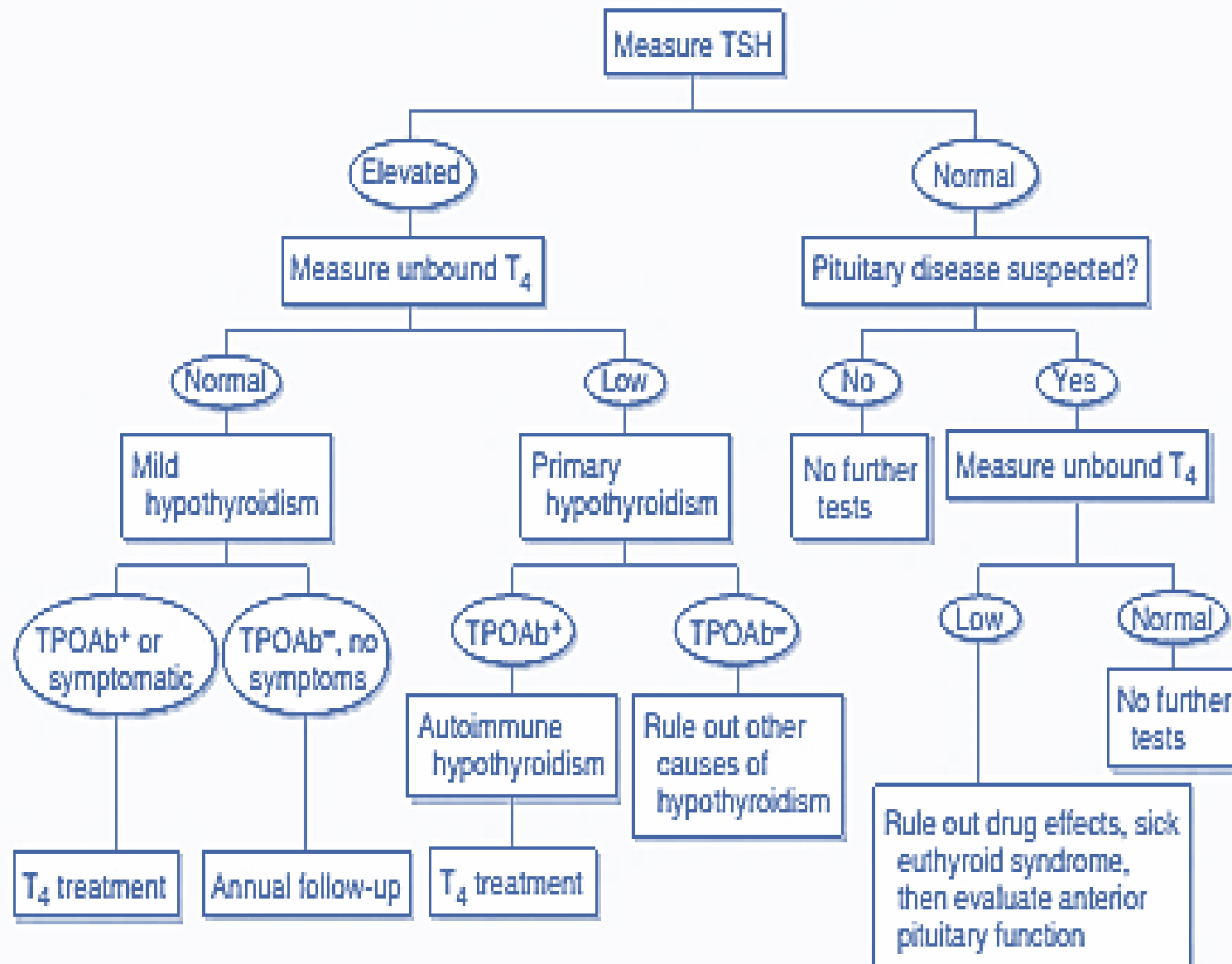
When T4 is lower than normal, always TSH is more than 10miu/ml

- **IN CASES THAT THIS RULE IS NOT SEEN; WHAT IS THE DIFF. DIGNOSIS:**

- ✓ *Central hypothyroidism*
- ✓ *Transition period from hyperthyroidism to Hypothyroidism*
- ✓ *Decreased TBG*
- ✓ *SES*



EVALUATION OF HYPOTHYROIDISM



- ❖ **T3 is the last parameters that declines in hypothyroidism.**
- ❖ **If T3 is decreased but T4 is normal, what is diagnosis...?**

Non-Thyroidal Illness (SES)

- ✓ Very common in hospitalized patients...
- ✓ Low T3 is the hallmark of TFT...
- ✓ T4 may be normal (usually), low or mildly high
- ✓ TSH may be normal (usually), low or mildly high (usually <10 mIU/l)



TFT IN HYPERTHYROIDISM

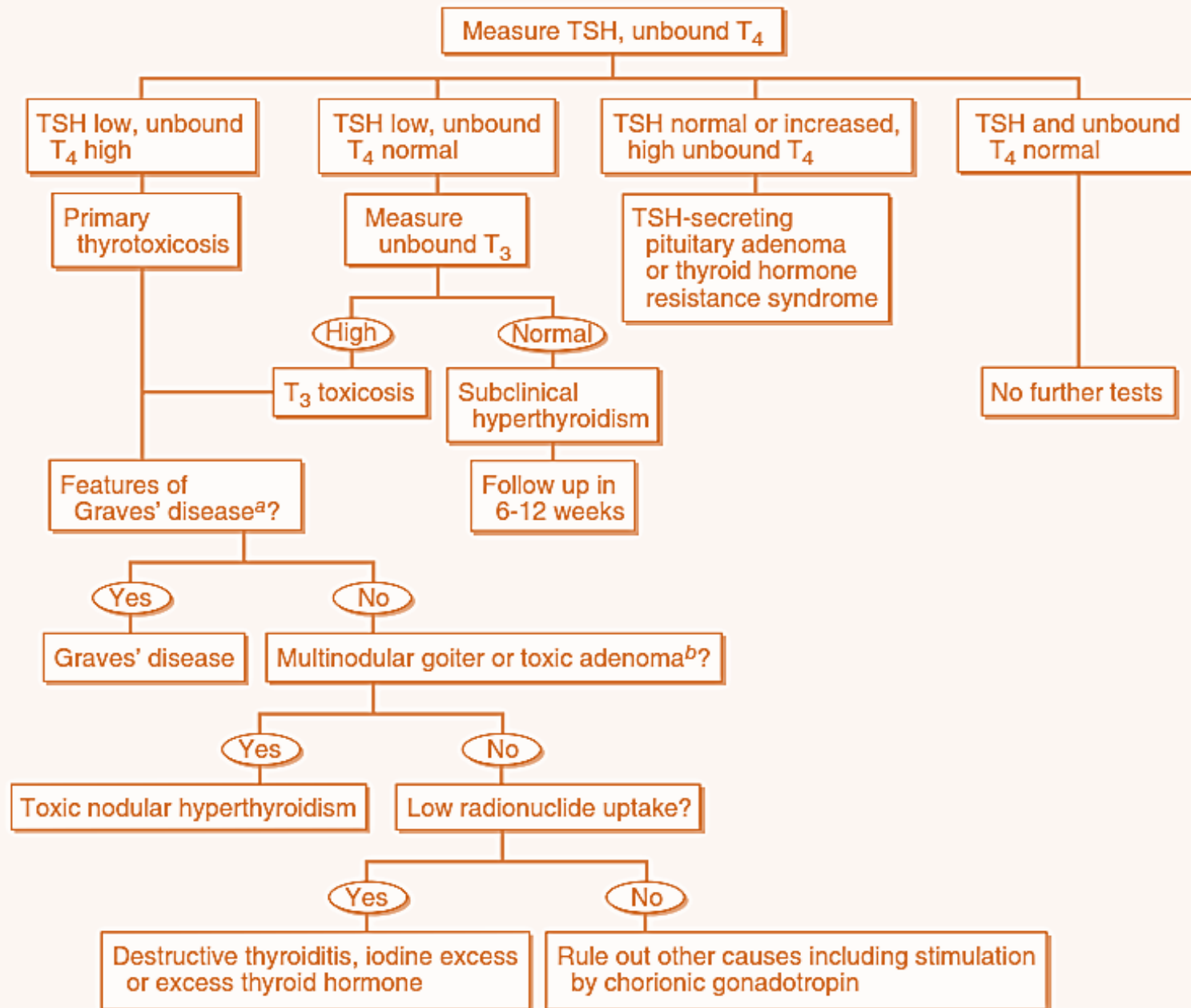
Suppressed TSH is the earliest change in hyperthyroid TFT...

➤ IF T4 IS ABOVE NL BUT TSH IS NOT SUPPRESSED WHAT IS DIFF. DIAGNOSIS...?

- ✓ Antibodies (resolution: use of other lab method ...)
- ✓ T4 treatment in hypothyroid patient (history)
- ✓ TBG effect (T3RU...)
- ✓ Transition period (history)
- ✓ Familial dysalbuminemia (FreeT4 by dialysis ...)
- ✓ TSH secreting tumors or TRH ...



EVALUATION OF THYROTOXICOSIS



- TESTES MUST BE REQUESTED IN...

- ✓ Hypothyroidism diagnosis : TSH (or TSH & T4)
- ✓ Hypothyroidism follow up : TSH
- ✓ Hyperthyroidism diagnosis : TSH & T4 (or TSH & T4 & T3)
- ✓ Hyperthyroidism follow up: TSH & T4 & T3
- ✓ Inpatients : TSH & T4 & T3 & T3RU



CASES

T4=5-12 , T3=90-190 , TSH=0.5- 4.5 , T3RU=25-35%

- 1) T4=4 , T3=90 ,TSH=50 , T3RU=26%
- 2) T4=4 , T3=30 ,TSH=4 , T3RU =35%
- 3) T4=4 , T3=90 ,TSH=3 , T3RU=40%
- 4) T4=3, T3=80 ,TSH=8, T3RU=25%



HYPOTHYROIDISM



Causes of Hypothyroidism...

Primary

Autoimmune hypothyroidism: Hashimoto's thyroiditis, atrophic thyroiditis
Iatrogenic: ^{131}I treatment, subtotal or total thyroidectomy, external irradiation of neck for lymphoma or cancer

Drugs: iodine excess (including iodine-containing contrast media and amiodarone), lithium, antithyroid drugs, *p*-aminosalicylic acid, interferon α and other cytokines, aminoglutethimide, tyrosine kinase inhibitors (e.g., sunitinib)

Congenital hypothyroidism: absent or ectopic thyroid gland, dyshormonogenesis, TSH-R mutation

Iodine deficiency

Infiltrative disorders: amyloidosis, sarcoidosis, hemochromatosis, scleroderma, cystinosis, Riedel's thyroiditis

Overexpression of type 3 deiodinase in infantile hemangioma and other tumors

Transient

Silent thyroiditis, including postpartum thyroiditis

Subacute thyroiditis

Withdrawal of supraphysiologic thyroxine treatment in individuals with an intact thyroid

After ^{131}I treatment or subtotal thyroidectomy for Graves' disease

Secondary

Hypopituitarism: tumors, pituitary surgery or irradiation, infiltrative disorders, Sheehan's syndrome, trauma, genetic forms of combined pituitary hormone deficiencies

Isolated TSH deficiency or inactivity

Bexarotene treatment

Hypothalamic disease: tumors, trauma, infiltrative disorders, idiopathic

- The **WHO** estimates that about 2 billion people are iodine-deficient, based on urinary excretion data...
- In areas of iodine sufficiency; **autoimmune disease** (Hashimoto's thyroiditis) and **iatrogenic causes** are most common...



Neonatal hypothyroidism

- **Hypothyroidism** occurs in about **1 in 4000** newborns...and is due to:
 - thyroid gland **dysgenesis** in 80–85%
 - inborn **errors of thyroid hormone synthesis** in 10–15%
 - TSH-R **antibody-mediated** in 5% of affected newborns
- The developmental abnormalities are twice as common in **girls** and the majority of infants appear normal at birth, but **<10%** are diagnosed based **on clinical features**, which include:
 - ✓ prolonged jaundice,
 - ✓ feeding problems,
 - ✓ hypotonia,
 - ✓ enlarged tongue,
 - ✓ delayed bone maturation,
 - ✓ umbilical hernia...



TABLE 405-1 GENETIC CAUSES OF CONGENITAL HYPOTHYROIDISM

Defective Gene Protein	Inheritance	Consequences
PROP-1	Autosomal recessive	Combined pituitary hormone deficiencies with preservation of adrenocorticotrophic hormone
PIT-1	Autosomal recessive Autosomal dominant	Combined deficiencies of growth hormone, prolactin, thyroid-stimulating hormone (TSH)
TSH β	Autosomal recessive	TSH deficiency
TTF-1 (TITF-1)	Autosomal dominant	Variable thyroid hypoplasia, cho- reoathetosis, pulmonary problems
TTF-2 (FOXE-1)	Autosomal recessive	Thyroid agenesis, choanal atresia, spiky hair
PAX-8	Autosomal dominant	Thyroid dysgenesis
TSH-receptor	Autosomal recessive	Resistance to TSH
G _{sα} (Albright hereditary osteodystrophy)	Autosomal dominant	Resistance to TSH
Na ⁺ /I ⁻ symporter	Autosomal recessive	Inability to transport iodide
DUOX2 (THOX2)	Autosomal dominant	Organification defect
DUOXA2	Autosomal recessive	Organification defect
Thyroid peroxidase	Autosomal recessive	Defective organification of iodide
Thyroglobulin	Autosomal recessive	Defective synthesis of thyroid hormone
Pendrin	Autosomal recessive	Pendred syndrome: sensorineural deafness and partial organification defect in thyroid
Dehalogenase 1	Autosomal recessive	Loss of iodide reutilization

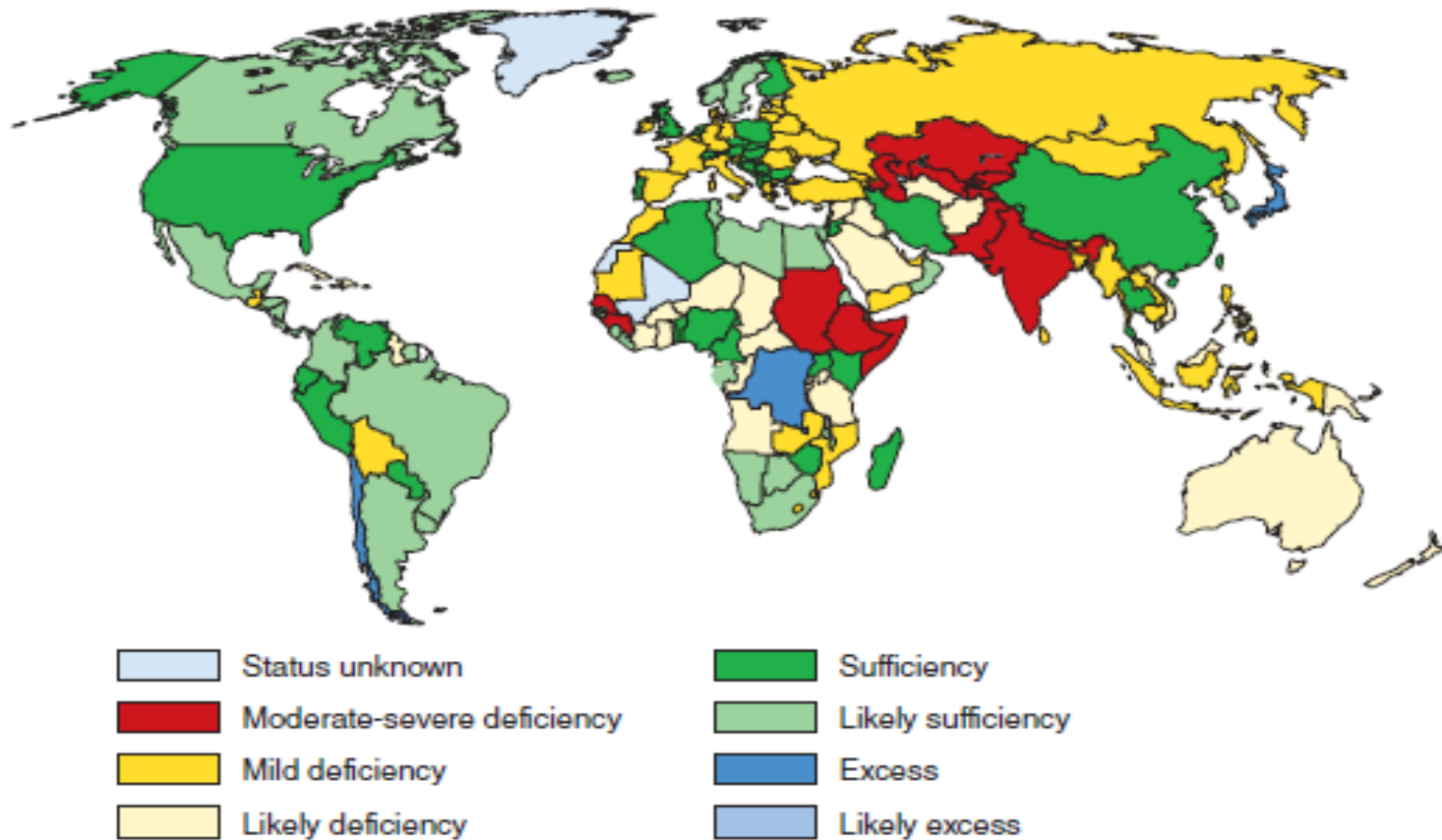
- These are generally based on measurement of TSH or T4 levels in **heel-prick** blood specimens...



- **T4** is instituted (after diagnosis), at a dose of 10–15 µg /kg per day, and the dose is adjusted by **close monitoring** of TSH levels...
- T4 requirements are relatively great during the **first year** of life... early treatment with T4 results in normal IQ levels, but subtle **neuro-developmental abnormalities** may occur in:
 - i. With the most severe hypothyroidism at diagnosis
 - ii. When treatment is delayed or suboptimal...



- Iodine **deficiency** remains a common cause of hypothyroidism **worldwide...**



- In areas of relative iodine deficiency, there is an increased prevalence of goiter and, when deficiency is severe, hypothyroidism and cretinism...



- Iodine **supplementation** of salt, bread, and other food substances has markedly reduced the prevalence of cretinism...
- In addition to overt **cretinism**, mild iodine deficiency can lead to subtle reduction of IQ...
- The recommended **average daily intake of iodine** is 150–250 µg/d for adults, 90–120 µg/d for children, and 250 µg/d for pregnant and lactating women...
- Urinary iodine is **> 10 µg/dL** in iodine-sufficient populations...



Autoimmune Hypothyroidism

- There is a marked **lymphocytic infiltration** of the thyroid with germinal center formation in Hashimoto's thyroiditis ...
- The mean **annual incidence** rate of autoimmune hypothyroidism is up to 4 per 1000 women and 1 per 1000 men.
- It is more common in certain populations, such as the Japanese, probably because of genetic factors and chronic exposure to a high-iodine diet...
- The mean age at diagnosis is 60 years, and the prevalence of overt hypothyroidism increases with age...
- Subclinical hypothyroidism is found in **6–8% of** women and **3% of** men... And the annual risk of developing clinical hypothyroidism is about 4% **when** subclinical hypothyroidism is associated with positive **TPO antibodies**...



- Antibodies to TPO and Tg are clinically **useful markers** of thyroid autoimmunity, but any pathogenic effect is restricted to a secondary role in amplifying an ongoing autoimmune response.
- Up to 20% of patients with autoimmune hypothyroidism have **antibodies against the TSH-R**, and these antibodies, cause hypothyroidism and, especially in **Asian** patients, thyroid atrophy...
- HLA-DR **polymorphisms** are the best documented genetic risk factors for autoimmune hypothyroidism, especially HLA-DR3, DR4, and -DR5 in Caucasians...
- A weak association also exists between polymorphisms in **CTLA-4**, a *T* cell–regulatory gene, and autoimmune hypothyroidism.



Clinical Manifestations



- Symptoms become more readily apparent at usually **TSH >10 mIU/L...**

TABLE 405-6 SIGNS AND SYMPTOMS OF HYPOTHYROIDISM (DESCENDING ORDER OF FREQUENCY)

Symptoms	Signs
Tiredness, weakness	Dry coarse skin; cool peripheral extremities
Dry skin	Puffy face, hands, and feet (myxedema)
Feeling cold	Diffuse alopecia
Hair loss	Bradycardia
Difficulty concentrating and poor memory	Peripheral edema
Constipation	Delayed tendon reflex relaxation
Weight gain with poor appetite	Carpal tunnel syndrome
Dyspnea	Serous cavity effusions
Hoarse voice	
Menorrhagia (later oligomenorrhea or amenorrhea)	
Paresthesia	
Impaired hearing	



Treatment

- Adult patients under 60 years old **without** evidence of heart disease may be started on 50–100 µg levothyroxine (T4) daily...
- **Adjustment** of levothyroxine dosage is made in **12.5-** or **25-µg** increments if the TSH is high...
- In the elderly, especially patients with known coronary artery disease, the **starting dose** of levothyroxine is **12.5–25 µg/d** with similar increments every 2–3 months until TSH is normalized...
- The **goal** of treatment being a **normal TSH**, ideally in the lower half of the reference range...
- Patients may not experience **full relief** from symptoms until **3–6 months** after normal TSH levels are restored.



- In patients of normal body weight who are **taking ≥ 200 μg** of levothyroxine per day, an elevated TSH level is often a sign of **poor adherence** to treatment...
- Other causes of **increased levothyroxine requirements** must be excluded:
 - ✓ Malabsorption (e.g., celiac disease, small-bowel surgery),
 - ✓ Ingestion with a meal...,
 - ✓ Drugs that interfere with T4 absorption or metabolism...
 - ✓ Estrogen or selective estrogen receptor modulator therapy



Myxedema

- Myxedema coma still has a **20–40% mortality** rate, despite intensive treatment, and outcomes are independent of the T4 and TSH levels.
- Myxedema coma **almost always** occurs in the **elderly** and is usually precipitated by factors that impair respiration, such as drugs, pneumonia, CHF, MI, GIB or CVA...
- Hypoventilation, leading to hypoxia and hypercapnia, plays a major role in pathogenesis and hypoglycemia & dilutional hyponatremia also contribute to the development of myxedema coma...
- **Clinical manifestations** include reduced level of consciousness, sometimes associated with seizures, as well as the other features of hypothyroidism...



- Levothyroxine can initially be administered as a **single** IV bolus of 500 µg, which serves as a loading dose and it's usually continued at a dose of 50–100 µg/d...
- If suitable IV preparation is not available, the same initial dose of levothyroxine can be given **by NGT**....
- Another option is to combine levothyroxine (200 µg) + liothyronine (25 µg) as a single, **initial IV bolus** followed by daily treatment...
- An alternative is to give liothyronine (T3) intravenously or via nasogastric tube (ranging from 10 to 25 µg every 8–12 h...) and this treatment has been advocated because $T4 \rightarrow T3$ conversion is impaired in myxedemacoma...



- **Supportive therapy** should be provided to correct any associated metabolic disturbances...
 - Any **precipitating factors** should be treated, including the early use of broad-spectrum antibiotics...
 - External **warming** is indicated only if the temperature is $<30^{\circ}\text{C}$...
 - Parenteral **hydrocortisone** (50 mg every 6 h) should be administered...
 - **Hypertonic saline** or IV **glucose** may be needed if there is severe hyponatremia or hypoglycemia...
 - **Ventilatory support** with regular blood gas analysis is usually needed during the first 48 h...





THYROTOXICOSIS

- **Thyrototoxicosis** is defined as the state of thyroid hormone excess and is not synonymous with **hyperthyroidism**, which is the result of excessive thyroid function...

Symptoms	Signs ^a
Hyperactivity, irritability, dysphoria	Tachycardia; atrial fibrillation in the elderly
Heat intolerance and sweating	Tremor
Palpitations	Goiter
Fatigue and weakness	Warm, moist skin
Weight loss with increased appetite	Muscle weakness, proximal myopathy
Diarrhea	Lid retraction or lag
Polyuria	Gynecomastia
Oligomenorrhea, loss of libido	

^aExcludes the signs of ophthalmopathy and dermopathy specific for Graves' disease.



TABLE 405-7 CAUSES OF THYROTOXICOSIS

Primary Hyperthyroidism

Graves' disease
Toxic multinodular goiter
Toxic adenoma
Functioning thyroid carcinoma metastases
Activating mutation of the TSH receptor
Activating mutation of $G_{\alpha s}$ (McCune-Albright syndrome)
Struma ovarii
Drugs: iodine excess (Jod-Basedow phenomenon)

Thyrotoxicosis Without Hyperthyroidism

Subacute thyroiditis
Silent thyroiditis
Other causes of thyroid destruction: amiodarone, radiation, infarction of adenoma
Ingestion of excess thyroid hormone (thyrotoxicosis factitia) or thyroid tissue

Secondary Hyperthyroidism

TSH-secreting pituitary adenoma
Thyroid hormone resistance syndrome: occasional patients may have features of thyrotoxicosis
Chorionic gonadotropin-secreting tumors^a
Gestational thyrotoxicosis^a

GRAVES' DISEASE

- Graves' disease accounts for **60–80% of thyrotoxicosis** and occurs in up to **2% of women** but is one-tenth as frequent in men...
- The disorder rarely begins before adolescence and typically occurs between **20 and 50 years** of age.
- A combination of **environmental** and **genetic** factors (polymorphisms in HLA-DR, the immunoregulatory genes CTLA-4, CD25, PTPN22, FCRL3, and CD226, as well as the TSH-R)...contribute to Graves' disease susceptibility...
- The concordance for Graves' disease in **monozygotic** twins is **20-30%** compared to <5% in dizygotic twins.



- **Smoking** is a minor risk factor for Graves' disease and a major risk factor for the development of ophthalmopathy.
- Sudden increases in **iodine intake** may precipitate Graves' disease, and there is a three-fold increase in the occurrence of Graves' disease in the postpartum period...
- Graves' disease may occur during the **immune reconstitution** phase after highly active antiretroviral therapy (HAART) or ...
- The hyperthyroidism of Graves' disease is caused by TSI that are synthesized in the **thyroid gland** as well as in **bone marrow** and **lymph nodes**....
- In particular, **TPO antibodies** occur in up to **80%** of cases and serve as a readily measurable marker of autoimmunity.



- The **clinical presentation** depends on ;
 - ✓ the severity of thyrotoxicosis,
 - ✓ the duration of disease,
 - ✓ individual susceptibility to excess thyroid hormone,
 - ✓ the patient's age...

- In the **elderly**, features of thyrotoxicosis may be subtle or masked, and patients may present mainly with **fatigue** and **weight loss**, a condition known as **apathetic** thyrotoxicosis...



FIGURE 405-8 Features of Graves' disease. **A.** Ophthalmopathy in Graves' disease; lid retraction, periorbital edema, conjunctival injection, and proptosis are marked. **B.** Thyroid dermopathy over the lateral aspects of the shins. **C.** Thyroid acropachy.

TREATMENT

- The main anti-thyroid drugs are :
 - **Thionamides** :
 - ✓ Propylthiouracil (PTU),
 - ✓ Carbimazole (not available in the United States),
 - ✓ Methimazole (active metabolite)
 - **Propranolol** (20-40 mg every 6 h)
 - **Radioiodine...**
- There is a small risk of thyrotoxic crisis after radioiodine, which can be minimized by pretreatment with **anti-thyroid** drugs for at least **a month** before treatment...



- Some patients with mild Graves' disease experience **spontaneous** relapses and remissions.
- About **15%** of patients who enter remission after treatment develop **hypothyroidism** 10–15 years later as a result of the destructive autoimmune process.
- Rarely, there may be fluctuation between hypothyroidism and hyperthyroidism due to changes in the functional activity of TSH-R antibodies...
- The **clinical course** of ophthalmopathy does **not follow** that of the thyroid disease... and anti-thyroid drugs or surgery have no adverse effects on the clinical course of ophthalmopathy.
- **Radioiodine** treatment for hyperthyroidism worsens the eye disease in a small proportion of patients (especially smokers)...



Thyroid storm

- Thyrotoxic **crisis** is usually **precipitated by** acute illness (stroke, infection, trauma, diabetic ketoacidosis), surgery (especially on the thyroid), or radioiodine treatment of **a patient with** partially treated or untreated hyperthyroidism.
- With life threatening exacerbation of hyperthyroidism, **accompanied** by fever, delirium, seizures, coma, vomiting, diarrhea, and jaundice.
- The **mortality rate** (as high as 30% even with treatment) due to:
 - Cardiac failure,
 - Arrhythmia,
 - Hyperthermia



Management of thyrotoxic crisis

- **Propylthiouracil** (500–1000 mg loading dose and 250 mg every 4 h)
- One hour after the first dose of propylthiouracil, stable **iodide** is given to block thyroid hormone synthesis via the Wolff-Chaikoff effect...
- **Propranolol** (although other β -adrenergic blockers can be used, high doses of propranolol decrease $T4 \rightarrow T3$ conversion, and the doses can be easily adjusted)...
- Short-acting IV esmolol can be used to decrease heart rate while monitoring for signs of heart failure.
- Additional therapeutic measures include **hydrocortisone** 300 mg IV bolus, then 100 mg every 8 h), **antibiotics** if infection is present, **cooling**, **oxygen**, and **IV fluids**...



THYROIDITIS

Acute

Bacterial infection: especially *Staphylococcus*, *Streptococcus*, and *Enterobacter*

Fungal infection: *Aspergillus*, *Candida*, *Coccidioides*, *Histoplasma*, and *Pneumocystis*

Radiation thyroiditis after ^{131}I treatment

Amiodarone (may also be subacute or chronic)

Subacute

Viral (or granulomatous) thyroiditis

Silent thyroiditis (including postpartum thyroiditis)

Mycobacterial infection

Drug induced (interferon, amiodarone)

Chronic

Autoimmunity: focal thyroiditis, Hashimoto's thyroiditis, atrophic thyroiditis

Riedel's thyroiditis

Parasitic thyroiditis: echinococcosis, strongyloidiasis, cysticercosis

Traumatic: after palpation

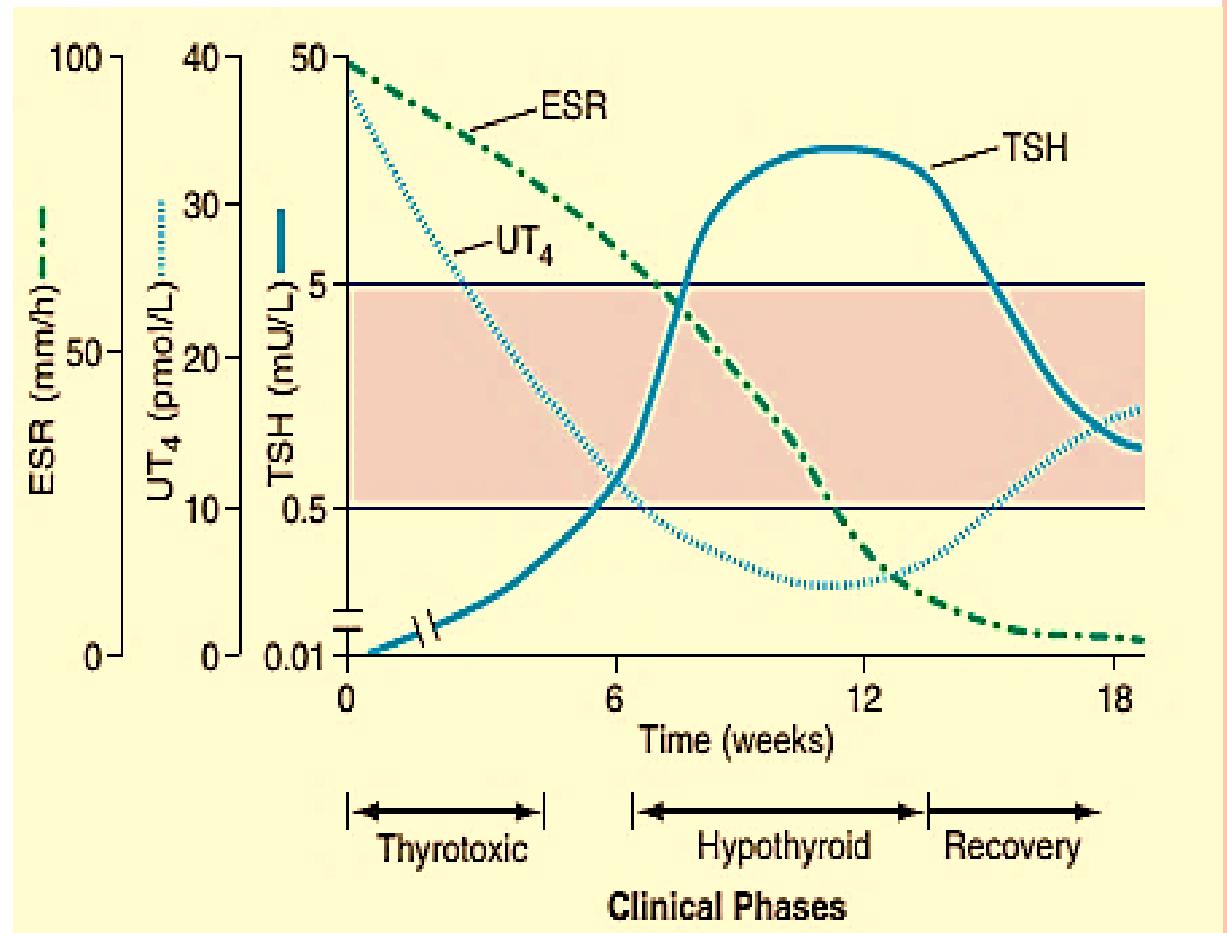


SUBACUTE THYROIDITIS

- The patient usually presents with a **painful** and **enlarged** thyroid, sometimes accompanied by fever....
- It's also **termed** de Quervain's thyroiditis, granulomatous thyroiditis, or viral thyroiditis (mumps, coxsackie, influenza, adenoviruses, and echoviruses...)
- The peak **incidence** occurs at **30–50 years**, and women are affected three times more frequently than men.
- The thyroid shows a patchy inflammatory infiltrate with disruption of the thyroid follicles and **multinucleated giant cells** within some follicles...
- Finally, the thyroid returns to normal, usually several months after onset.



- The release of thyroid hormones is initially associated with a **thyrotoxic phase** and suppressed TSH... **hypothyroid phase** then ensues, with low T4 and TSH levels that are initially low but gradually increase...



- The **diagnosis** is confirmed by a **high ESR** and **low uptake** of radioiodine (<5%) or 99mTc pertechnetate (as compared to salivary gland pertechnetate concentration).
- The white blood cell count may be increased, and thyroid antibodies are negative...
- If the diagnosis is in doubt, **FNA biopsy** may be useful, particularly to distinguish unilateral involvement from bleeding into a cyst or neoplasm.
- 600 mg of **aspirin** every 4–6 h or NSAIDs are sufficient to control symptoms in many cases...
- 40–60 mg of **prednisone**, depending on severity (gradually **tapered** over 6–8 weeks, in response to improvement in symptoms and the ESR...)



SILENT THYROIDITIS

- Painless thyroiditis, or “silent” thyroiditis, occurs in patients with **underlying autoimmune** thyroid disease....
- Clinical course similar to that of subacute thyroiditis...and as in subacute thyroiditis, the uptake of ^{99m}Tc pertechnetate or radioactive iodine is initially suppressed.
- The condition occurs in up to **5%** of women 3–6 months after pregnancy and is then termed postpartum thyroiditis.
- Typically, patients have a brief phase of thyrotoxicosis lasting 2–4 weeks, **followed by hypothyroidism for 4–12 weeks**, and then resolution; often, however, only one phase is apparent...



- Differentiated with :
 - 1) Painless goiter...
 - 2) Normal ESR and the &
 - 3) Presence of TPO antibodies...
- Glucocorticoid treatment is not indicated for silent thyroiditis...
- Propranolol, 20–40 mg three or four times daily.
- Thyroxine replacement may be needed for the hypothyroid phase but should be withdrawn after 6–9 months, as recovery is the rule.
- Annual follow-up thereafter is recommended...
- The condition may recur in subsequent pregnancies.



